



## Case Report

# Hypersensitivity Pneumonitis Caused by *Mucor* Species in a Cork Worker

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## ABSTRACT

Suberosis is a type of hypersensitivity pneumonitis caused by exposure to cork proteins and molds such as *Aspergillus fumigatus* and *Penicillium frequentans*. We present the case of a man with suberosis caused by *Mucor* species, a mold that has been rarely reported to cause hypersensitivity pneumonitis. Furthermore, the patient had symptoms and lung function tests indicating bronchial obstruction—an atypical presentation of hypersensitivity pneumonitis. No imaging abnormalities were observed. A diagnosis was made on the basis of bronchoalveolar lavage and transbronchial biopsy findings. *Mucor* species was identified as the causative agent using a specific bronchial challenge test.

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## Neumonitis por hipersensibilidad a *Mucor* sp. en un trabajador de la industria del corcho

## RESUMEN

La suberosis es un tipo de neumonitis por hipersensibilidad causada por la exposición a proteínas propias del corcho y a hongos tales como *Aspergillus fumigatus* y *Penicillium frequentans*. Presentamos el caso de un varón afectado de suberosis en quien el agente implicado fue *Mucor* sp., hongo hasta ahora prácticamente no descrito como causante de neumonitis por hipersensibilidad. Además, se trata de un caso con una presentación clínica atípica, que comenzó con síntomas y pruebas de función pulmonar en forma de obstrucción, y en el que no se evidenciaron alteraciones en las pruebas de imagen. El diagnóstico se obtuvo a partir de los resultados del análisis del lavado broncoalveolar y de una biopsia transbronquial. La identificación del agente responsable se realizó por medio de una prueba de provocación bronquial específica.

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## Introduction

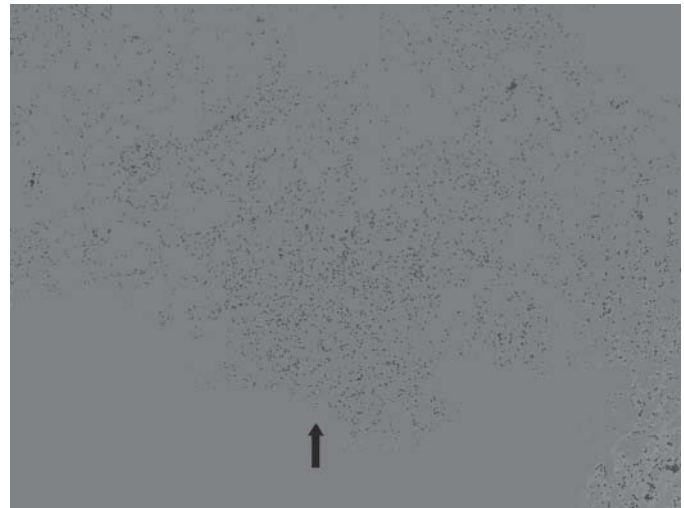
Hypersensitivity pneumonitis refers to a heterogeneous group of lung diseases characterized by an abnormal immune reaction to antigens contained in a wide variety of organic dusts.<sup>1</sup> The list of diseases and antigens involved in the genesis of hypersensitivity pneumonitis has continued to grow since farmer's lung was first described in 1932; the most common are farmer's lung, bird fancier's lung, espartosis, and suberosis.<sup>2</sup> In the specific case of suberosis, cork proteins and molds such as *Aspergillus fumigatus* and *Penicillium frequentans*<sup>3</sup> have been implicated in the development of the disease. We present the case of a 44-year-old male cork worker with suberosis caused by *Mucor* species. The clinical presentation was bronchial obstruction, which is rarely seen in hypersensitivity pneumonitis.

## Case Description

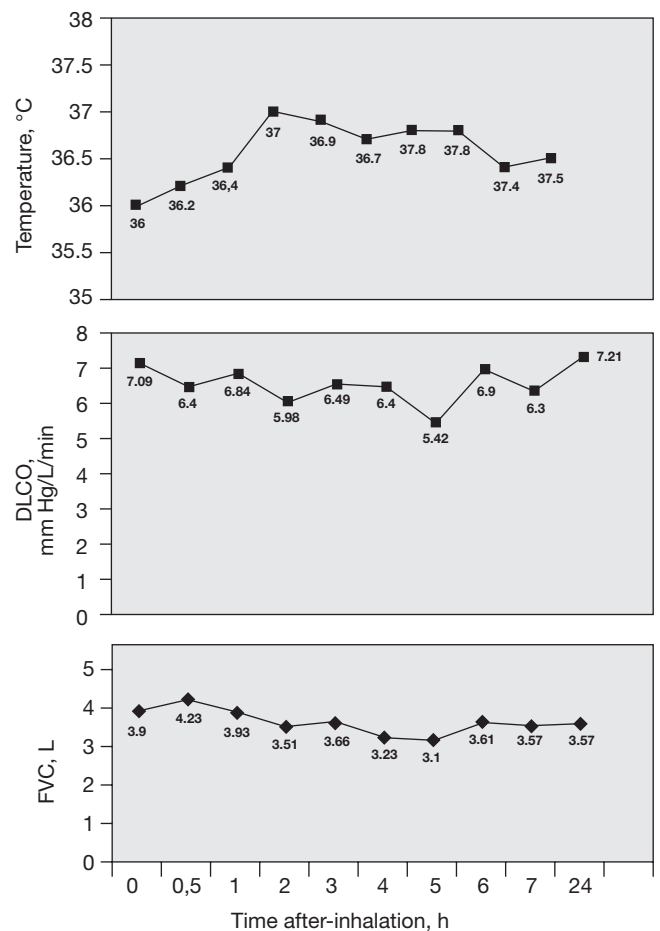
The patient, a 44-year-old man with a smoking history of 5 pack-years ending more than 15 years ago and no other relevant history, had worked in the cork industry for the past 15 years, both in manufacturing and in handling of raw material. Three years before consultation, he started to present progressively worsening dry cough, exertional dyspnea, and wheezing, symptoms that he related to occupational exposure and that improved on the weekends and during holidays. He also presented occasional rhinitis and conjunctivitis. Auscultation revealed wheezing in both lung fields; the rest of the physical examination was normal. Blood tests showed 11 200 leukocytes (78% neutrophils, 13% lymphocytes, 1.3% eosinophils, and 6.6% monocytes), a hematocrit of 50%, and total immunoglobulin (Ig) E of 40 U/L. Specific tests for IgE against common airborne allergens and IgG against *Mucor mucedo*, *A fumigatus*, *P frequentans*, and cork proteins were negative. The chest radiograph and computed tomography (CT) scan were normal. Pulmonary function testing revealed a moderate to severe obstructive ventilatory disorder, with a forced vital capacity (FVC) of 3.32 L (72%), forced expiratory volume in 1 second (FEV<sub>1</sub>) of 2.07 L (55%), and FEV<sub>1</sub>/FVC of 62%. The total lung capacity was 6.11 L, and the residual volume was 2.74 L (149%). A transfer factor test showed a moderate decrease in carbon monoxide diffusing capacity (DLCO), which was 4.96 mmol/min/kPa (48%); the ratio of DLCO to alveolar volume was 0.97 mmol/min/kPa/L (51%). The bronchodilator test was negative, whereas a culture of the patient's sputum and of a cork sample from the workplace were both positive for *Mucor*. A skin prick test for *M mucedo*, *P frequentans*, *A fumigatus*, and cork proteins was negative, but intradermal reaction testing at a concentration of 1/10 of *M mucedo*, *A fumigatus*, and cork proteins caused indurations of 14×16, 11×14, and 9×11, respectively, 15 minutes after the injections. Because hypersensitivity pneumonitis was suspected, fiberoptic bronchoscopy was performed but the bronchial aspirate obtained was negative for malignant cells. The bronchoalveolar lavage fluid showed 42% macrophages, 32% lymphocytes, and 26% polymorphonuclear cells. A transbronchial biopsy revealed moderate chronic lymphocytic interstitial pneumonitis, with nonnecrotizing granulomas (Figure 1). A specific bronchial challenge test for *M mucedo* was positive (Figure 2). Once suberosis was diagnosed, the patient was advised to stay away from his workplace, and his clinical symptoms gradually improved. Six months later, the patient showed improvement in pulmonary function, with a FVC of 4.20 L (91%), FEV<sub>1</sub> of 2.60 L (73%), FEV<sub>1</sub>/FVC of 61%, DLCO of 62%, and a ratio of DLCO to alveolar volume of 60% of the theoretical value.

## Discussion

The present case demonstrates that *Mucor* species can cause hypersensitivity pneumonitis. This agent has only been implicated in



**Figure 1.** Transbronchial biopsy. Septal thickening, moderate lymphocytic infiltrate, and caseating granuloma (arrow) are observed.



**Figure 2.** Specific bronchial challenge test for *Mucor mucedo* at a concentration of 1/10. The test was considered positive because of a decrease of 18% in forced vital capacity (FVC) and of 24% in carbon monoxide diffusing capacity (DLCO), and an increase of 1°C in temperature.

1 case of hypersensitivity pneumonitis caused by inhalation of misting-fountain vapors along with other agents such as *Bacillus subtilis* and *Saccharomyces cerevisiae*.<sup>4</sup> In the specific case of suberosis,

the causative agents reported to date have been cork proteins, *P frequentans*, and *A fumigatus*.<sup>3</sup> Our group had previously suggested that *Mucor* and *Rhizopus* species, in addition to cork, might be implicated in the development of suberosis,<sup>3</sup> but this had not been proven until now. Although in the present case the intradermal reaction was positive for *M mucedo*, *A fumigatus*, and cork proteins in this patient, we suspected *Mucor* because it was the only mold isolated in the culture of cork taken from the patient's workplace and because it was also isolated in the sputum culture. The positive bronchial challenge test to *Mucor* clearly demonstrated its involvement in the etiology of this disease, although we cannot rule out the implication of the other 2 agents because we did not perform specific bronchial challenge tests.

Another atypical aspect of our case was the clinical presentation. In fact, the initial clinical picture (dry cough, wheezing, and exertional dyspnea related to the patient's occupation) was suggestive of bronchial asthma or chronic obstructive pulmonary disease. In addition, pulmonary function testing showed moderate to severe occlusion. However, the bronchodilator test was negative, the DLCO had dropped considerably (and was not corrected for alveolar volume), and the chest radiograph and CT scan were completely normal. Although bronchial obstruction is an atypical clinical presentation in hypersensitivity pneumonitis, several reports suggest that it is not rare.<sup>5-7</sup> Indeed, a recently published series of 86 patients found that restrictive ventilatory impairment was the most common functional pattern in bird fancier's hypersensitivity pneumonitis, but that 13% of patients had bronchial obstruction,<sup>8</sup> which, in more advanced stages of the disease, may develop into emphysema, as has been seen in patients with farmer's lung.<sup>9</sup>

In our patient, the decrease in DLCO and the normal chest CT scan suggested hypersensitivity pneumonitis, a diagnosis confirmed by the bronchoalveolar lavage fluid and transbronchial biopsy findings. Although a decrease in DLCO is typical in hypersensitivity pneumonitis and can be considered an important predictor of disease outcome,<sup>8</sup> the same is not true of the chest CT scan. The most common radiologic findings in hypersensitivity pneumonitis are

ground-glass opacities and micronodules in the subacute forms of the disease, and air-trapping in expiratory studies.<sup>5,10</sup> Increased linear density (84%), honeycombing (16%), and traction bronchiectasis are more or less characteristic findings in the chronic forms of the disease.<sup>11,12</sup> A normal CT scan is observed in up to 16% of patients.<sup>1</sup>

In conclusion, *Mucor* species may be implicated in some cases of suberosis and should be taken into account when assessing the various types of hypersensitivity pneumonitis. Furthermore, although atypical, hypersensitivity pneumonitis may be diagnosed even when the radiologic findings are normal and the symptoms and breathing pattern indicate obstruction.

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